REMARKS

Status of Claims

In the Office Action, the Examiner indicated that claims 24-68 are pending in the application and the Examiner rejected all claims. Claims 46, 52, and 66, however, were canceled in the Reply dated December 1, 2006. Claim 24 has been amended. No claims have been canceled or added in the present Reply. Accordingly, Claims 24-45, 47 to 51, 53-65, and 67-68 are pending.

Inconsistencies in Action

(1) Although Claims 26, 45 and 54 were indicated as rejected on the Office Action Summary (PTOL-326), the claims were not addressed in the body of the Action.

(2) Paragraph 7 (page 7) of the action indicated that claim 49 was being rejected under 35 U.S.C. § 103(a) as being unpatentable over Barry (U.S. Patent No. 5,991,729) in view of Huyn (U.S. Patent Application Publication 2002/0035486). Subparagraphs B, C, E, F, G, and H (there is no subparagraph D), however, refer to a combination of Barry in view of Tacklind (U.S. Patent No. 5,626,144). Likewise, paragraph 10 refers to the rejection of claim 49 as being Barry in view of Tacklind.

In view of the above, on May 14, 2007, applicants' attorney, Marc Segal, called the Examiner to determine how to proceed. The Examiner indicated that the rejections stated in subparagraphs B, C, E, F, G, and H of paragraph 7, and paragraph 10 should be based on the combination of Barry in view of Huyn rather than Barry in view of Tacklind. In view of these corrections, the Examiner agreed that the next Action would not be made final.

Summary of Claim Amendment

Claim 24 has been amended to clarify that the donor in step (a) is from "a collection establishment." Support can be found at paragraph 15 of the application as published. No new matter has been added.

Claimed Invention

The claimed invention relates to a method for identifying a research subject in a group of donors from a *collection establishment*. This method involves obtaining a biological sample and medical data from such donors to create a database from which research subjects can be identified by screening the database for identifying criteria. The claimed invention also relates to a method of creating a database by collecting a biological sample and medical data from a donor from a *collection establishment* that includes proteomic and genomic information from the sample. The claimed invention further relates to using this database to identify genomic and proteomic characteristics which correlate with a disease.

Applicants' claimed *methods leverage the sample and data collecting capabilities of collection establishments* which have not been traditionally involved in identifying research subjects. By using collection establishments to gather medical data and biological samples, the pharmaceutical industry can gain access to an ethnically diverse population that is not limited to patients suffering from particular diseases. Given that many donors are repeat donors, this method also allows for the collection of biological samples and medical data longitudinally. Another advantage of using collection establishments is that they typically have long-term sample storage infrastructure for storing biological samples. A database generated from longitudinal medical data and testing of longitudinal biological samples from a diverse population may help identify genomic and proteomic characteristics which correlate with a disease.

Discussion of Prior Art References

Each of the Examiner's obviousness rejections relies on U.S. Patent No. 5,991,729 to Barry et al. (Barry) in combination with one or more of the following patents U.S. Patent No. 6,368,797 to Schappert (Schappert); "Avandel Healthcare Selects ThinkMed to Support Early Identification and Medical Management of Patients with Catastrophic Diseases" (Avandel); U.S. Patent Application Publication 2002/0035486 to Huyn (Huyn); U.S. Patent No. 5,915,240 to Karpf (Karpf); and U.S. Patent No. 6,730,477 to Sun et al. (Sun). Although the Action cites to U.S. Patent No. 5,626,144 to Tacklind et al. (paragraphs 7 and 10), the Examiner has indicated that these citations should be to Huyn as discussed above.

These patents are each discussed in turn below in the order in which they were cited in the Examiner's Action.

U.S. Patent No. 5,991,729 to Barry et al.

U.S. Patent No. 5,991,729 to Barry et al. ("Barry") teaches methods for generating a document that contains medical information specific to a patient to aid in medical counseling. As shown in Figures 1 and 2, a biological sample is taken from a patient, analyzed, and a diagnostic code and a description of the analysis of the sample are entered into a relational database. A report can be generated from the database that retrieves archived textual and graphical information specific for the entered diagnostic code and compiles a report specific to a particular patient. Accordingly, Barry is directed to *method of creating an individualized medical report* based on entering a diagnostic code into a relational database which contains archived information for each diagnostic code. Barry is not directed to a method for creating a database of medical data from donors nor is Barry directed to a method for identifying research subjects from such a database.

U.S. Patent No. 6,368,797 to Schappert

U.S. Patent No. 6,368,797 to Schappert ("Schappert") teaches a method for treating or identifying patients at risk for neurological diseases, especially Alzheimer's, based on testing for allelic variants of GPIIIa or GPIIb and forecasting the outcome/suitability for entering patients into clinical drug trials. The invention in Schappert is based on the realization that patients with Alzheimer's were almost four times more likely to have mutations in both the GPIIIa and GPIIb allele. Schappert is not directed to creating a database of medical data from donors nor is Schappert directed to method for identifying a research subjects from such a database.

Avandel Healthcare Selects ThinkMed to Support Early Identification and Medical Management of Patients with Catastrophic Diseases

"Avandel Healthcare Selects ThinkMed to Support Early Identification and Medical Management of Patients with Catastrophic Diseases" (Avandel) is a Press Release from ThinkMed, LLC dated August 13, 1998. Avandel discloses using software to monitor patient data for "risk-bearing organizations" (i.e., insurance companies, HMOs) in order to "systematically plan, implement and monitor population heath management strategies." (Paragraph 6). The software allows insurance companies or HMOs to "intervene earlier in the clinical progression of various diseases" "to reduce costs, severity and frequency of catastrophic medical events to [their] customers." (Paragraph 3) Insurance companies and HMOs use this information for "early identification of at-risk patients and stratification of patients into clinically relevant groups." (Paragraph 4). These tools allow insurance companies to assess their risk. Avandel is not directed to a method for identifying criteria for selecting a research subject or identifying research subjects.

U.S. Patent Application Publication 2002/0035486 to Huyn

U.S. Patent Application Publication 2002/0035486 to Huyn (Huyn) teaches a computer implemented questionnaire system and method for obtaining clinical data from subjects. The

questions of the system are dynamically linked in dependence on previous responses received from the subject. The purpose of the system is to obtain broad, unbiased, and longitudinal data from patients. Huyn is not directed to creating a database of medical data and information from biological samples from donors nor is Huyn directed to method for identifying a research subjects from such a database.

Applicants note that Huyn published from an application filed on July 20, 2001. The present application claims the benefit of U.S. Provisional Application No. 60/227,910, filed August 28, 2000. Huyn claims the benefit of two U.S. Provisional Applications filed on July 21, 2000 and August 18, 2000. Accordingly, Huyn's priority date is only a month earlier than the present application. Because Huyn is being applied as a secondary reference to dependent claims which are non-obvious over the primary references, as discussed below, applicants have not challenged the availability of Huyn as a reference. Should any rejections over Huyn be maintained, applicants anticipate being able to antedate this reference by filing a Section 1.131 declaration.

U.S. Patent No. 5,915,240 to Karpf

U.S. Patent No. 5,915,240 to Karpf ("Karpf") teaches a reference computer system for access to medical information over a computer network. The network includes a number of elements: a medical look-up "client" program, a medical look-up "server" program, and a medical "call server". The server provides a central database for a single type of medical information. The client program maintains a local database for a variety of types of medical information. The client program automatically updates itself from the servers. A network chat facility (med call) allows the user to engage in real-time communication with a person at a help site who can provide assistance to the user. For example, the reference computer system can be used to look up medical information that must be up-to-date and current such as blood donor deferral criteria. Karpf does not teach creating a database of medical data from donors much less using such a database to identify research subjects.

U.S. Patent No. 6,730,477 to Sun et al.

U.S. Patent No. 6,730,477 to Sun et al. ("Sun") is directed to methods for diagnosing, monitoring and staging breast cancer based on analyzing changes in levels of breast specific genes (BSG) in cells. Sun does not teach creating a database of medical data from donors much less using such a database to identify research subjects.

Discussion of Claim Objection

Claim 49 was objected to because the Examiner considers the phrase "donor from a least one collection establishment" unclear. In the context of claim 49, the phrase is "collecting a biological sample from at least one donor from at least one collection establishment." The phrase requires at least one (i.e., one or more) donors (e.g., one who donates blood or plasma, see paragraph 15 of published application) from at least one (i.e., one or more) collection establishment (e.g., blood or plasma collection organizations, see paragraph 15 of published application). Thus, if more than one donor is used the donors can be from more than one collection establishment. Applicants submit respectfully that the claim is clear and, thus, request that this objection be withdrawn.

Claim 49 is also objected to because the Examiner asserts that it is not clear "how the step of deriving proteomic information and genomic information from the sample can be performed before a sample is collected from the donor." Claim 49 recites that steps (b) through (d) can be performed in any order. Step (a) directed to "collecting a biological sample", however, is performed before steps b through d. Accordingly, contrary to the Examiner's assertion, the claim recites that the sample is collected before being analyzed. Applicants submit respectfully that the claim is clear and, thus, request that this objection be withdrawn.

Discussion of Obviousness Rejections

Applicants submit that the Examiner has failed to establish a *prima facie* showing of obviousness, and that the claimed invention is patentably distinct over the references cited.

"To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP § 2143.

Here, the combination of references applied by the Examiner do not teach or suggest all the claim limitations. None of the art cited by the Examiner alone or in combination provides a method for identifying a research subject in a group of donors from at least one collection establishment or a method of creating a database by collecting a biological sample and medical data from a donor from a collection establishment that includes proteomic and genomic information from the sample. This is because the following art relied upon by the Examiner is directed to fundamentally different types of medical databases for fundamentally different purposes as summarized below:

Barry	a relational database for matching archived medical information to particular diagnosis codes and generating a specific patient report;
Schappert	a database of similarly afflicted subjects (Alzheimer's) containing the GPIIIa and GPIIb genotypes and other health data for determining how to treat a similarly afflicted patient;

Avandel	a database for early identification of at-risk patients and stratification of patients into clinically relevant groups (i.e., risk assessment);
Huyn	a database for storing subject responses to a medical questionnaire; and
Karpf	a database for storing up-to-date medical information that can be accessed by remote systems.

Each of the Examiner's rejections is addressed in turn below.

A. Claims 24, 28-30, 33-36, 38, 42-44 and 66-67

The Examiner has rejected Claims 24, 28-30, 33-36, 38, 42-44 and 66-67 under 35 U.S.C. § 103(a) as being unpatentable over Barry in view of Schappert and in further view of Avandel.

1. Neither Barry, Schappert nor Avandel collecting biological samples or medical data from donors of collection establishments

Claim 24, the only independent claim addressed by this rejection, is directed to a method for "identifying a research subject in a group of donors from at least one collection establishment" As amended, Claim 24 recites the step of "obtaining a biological sample and medical data from a donor from a collection establishment." Although applicants believe that the claim was clear prior to the above amendment, Claim 24 has been amended to clarify that the donor from step (a) is from a collection establishment.

None of the references cited discuss collecting biological samples and medical data from *donors of collection establishments* in order to generate a database for identifying research subjects. Although applicants believe that the claim was clear prior to the above amendment, Claim 24 has been amended to clarify that the donor from step (a) is from a collection establishment. As discussed in the specification, collection establishments refer to blood or

plasma organizations. (Paragraph 15 of application as published). None of the references even disclose collecting biological samples from such donors to be used in a database. Barry merely collects data from a single patient in order to generate a report specific to that patient. (Barry at column 4, line 9). Schappert discloses testing for specific variant alleles from those susceptible to neurological disorders. (Schappert at column 12, lines 34-36). Avandel is directed to analyzing medical data from customers of insurance companies or HMOs. (Avandel at paragraph 3).

Accordingly, because neither Barry, Schappert, nor Avandel disclose "obtaining a biological sample and medical data from a donor from a collection establishment," this obviousness rejection must be withdrawn.

2. Neither Barry, Schappert, nor Avandel disclose matching a donor's medical data with certain criteria for a research project

The cited art also fails to meet the claimed requirement of matching the donor's medical data with certain criteria for a research project. The Examiner concedes that Barry does not disclose "identifying criteria for selecting a research subject" or "extracting an identifier from the first database, wherein said identifier is associated with a donor matching the identified criteria." Office Action at p. 3. To overcome this gap, the Examiner cites to Col. 12, ln. 43-52 of Schappert which reads:

> Further, either alone or in combination with other health data, the variant GPIIIa and GPIIb alleles can be used to predict a subject's outcome by comparing the subjects GPIIIa and GPIIb genotypes (and other health data) to a patient database containing the GPIIIa and GPIIb genotypes (and other health data) of similarly afflicted subjects. Based on this database comparison, a subject's likely outcome, i.e., progression of disease, cure rate, response to therapy, morbidity and mortality, can be statistically assessed.

As seen in this quote, the focus is not on the identification of research subjects from a pool of donors from collection establishments as in claim 24, but instead on using genomic information from one subject and comparing this patient's genotype to a patient database of *similarly afflicted* subjects. In stark contrast, Claim 24 and its dependents are directed to identifying criteria for selecting a research subject and using these criteria to identify a matching donor. Conversely, Schappert uses its criteria (GPIIIa and GPIIb alleles) by comparing it to data from *similarly afflicted* subjects for prognosis/treatment of Alzheimer's disease. Thus, the method does not involve *identifying* research subjects by using certain criteria but rather taking an *already identified subject* and determining what therapies would be most efficacious by comparing certain criteria to similarly afflicted subjects. In view of the above, applicants respectfully request the Examiner to reconsider and withdraw the rejection.

3. Neither Barry, Schappert, nor Avandel disclose matching a research identifying criteria with a name and contact information in order to identify a research subject

The cited art also fails to disclose identifying a research subject as in step (f) of Claim 24. The Examiner concedes that "the combined teachings of Barry and Schappert do not teach that the purpose of the matching step (step (f)) is in order to identify a research subject nor do they teach certain criteria for a research project." Office Action at p. 4. To overcome this gap, the Examiner cites to Avandel as allegedly disclosing a means for identifying potentially high-risk and high-cost patients from querying medical data in a database. According to the Examiner, these high-risk and high-cost patients are then recommended for management interventions (e.g. clinical or research trials).

Applicants submit respectfully that the Examiner has misconstrued the teachings of Avandel. As discussed above, Avandel discloses using software to monitor patient data for "risk-bearing organizations" (i.e., insurance companies, HMOs, etc.) in order to "systematically plan, implement and monitor population heath management strategies." (Paragraph 6). While

the Examiner is correct in that high-risk patients are recommended for management interventions, Avandel does not disclose recommending these patients for clinical trial studies. In fact, nothing in Avandel discusses clinical or research trials. This is not surprising in that insurance companies and HMOs typically do not provide coverage for these types of experimental treatments. Insurance companies and HMOs use this data for "early identification of at-risk patients and stratification of patients into clinically relevant groups." In other words, the database of Avandel is used for risk assessment and risk reduction, not for identifying research subjects. Accordingly, Avandel does not disclose matching an identifying criteria for selecting a research subject with a name and contact information to identify a research subject.

Accordingly, for this additional reason, the rejection of Claim 24 and its dependent claims should be withdrawn.

4. Examiner's Response to Applicant's Argument

In the Action, the Examiner responds to applicants' previous Reply with the following:

> In addition, in response to applicant's argument that the previously used prior art references teach methods that are not used for identifying research subjects from a database of biological samples or patient medical data, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Action at paragraph 12. This does not make any sense. Applicants' claimed invention is directed to a *method* of identifying research subjects in a group of donors from at least one collection establishment. As such, applicant's claimed *methods* recite steps not structure. Moreover, as discussed above, not only do the references not disclose the intended use of the method – which is part of the body of the claim – the references do not teach all of the recited steps of the claimed method, namely collecting samples from donors from collections

establishments, identifying research criteria, extracting an identifier based on the identified criteria, and matching the identifier with the name and contact information of the donor.

B. Claim 25

The Examiner has rejected Claim 25 under 35 U.S.C. § 103(a) as being unpatentable over Barry in view of Schappert as applied to Claim 24 above.

Claim 25 is directed to the method of Claim 24 wherein informed consent is obtained from the donor. Since, as discussed above, the combination of Barry and Schappert does not teach or suggest the invention of Claim 24, it can not render obvious Claim 25 which depends on Claim 24. Accordingly, reconsideration and withdrawal of this rejection is requested respectfully.

C. Claims 47 and 48

The Examiner has rejected Claims 47 and 48 under 35 U.S.C. §103(a) as being unpatentable over Barry in view of Huyn.

Claim 48 is directed to the method of Claim 24 wherein the biological samples are associated with an identifier linking the donor and biological sample with the derived information about the sample, and the samples are collected and stored longitudinally. Claim 47 is directed to the method of Claim 48 wherein the biological sample is of the recited type.

The Examiner concedes that Barry "does not teach that the biological samples are collected and stored longitudinally." Office Action at p. 6. To overcome this gap, the Examiner cites paragraph 0088 of Huyn which reads:

> It is anticipated that the questionnaire will be used to collect longitudinal patient data, i.e., data from the same patient at regular or irregular time intervals. All time-varying data are preferably stored in the database. Data collected at a later time are referred to

> as later-time data. Preferably, when a subject completes the questionnaire for the second and subsequent times, the questionnaire appears with previous data entered. The user can then selectively change data reflecting modified symptoms without having to complete the entire questionnaire. In some cases, questions whose responses do not change (e.g., gender, for most subjects) are not presented at subsequent sessions.

As can be seen above, this portion of Huyn does not teach collecting biological samples much less biological samples that are collected and stored longitudinally. Rather, Huyn teaches that answers to the medical questionnaire can be collected at subsequent times. As discussed above, applicants have leveraged blood or plasma *collection establishments* to collect biological samples *from donors* longitudinally.

Moreover, since, as discussed above, the combination of Barry and Schappert does not teach or suggest the invention of Claim 24, even if Huyn discloses the additional limitation of applicants' dependent Claims 47 and 48 – which it does not – its combination with Barry still would not render obvious the claimed invention. Huyn does not teach or suggest using donors from a collection establishment to gather biological samples and medical data for use in identifying research subjects. Accordingly, reconsideration and withdrawal of this rejection is requested respectfully.

D. Claims 49-51, 53, and 59-61

The Examiner has rejected Claims 49-51, 53, and 59-61under 35 U.S.C. §103(a) as being unpatentable over Barry in view of Huyn. As discussed above, although the Action states that the rejection of Claims 50-51, 53, and 59-61 are being made over Barry in view of Tacklind, the Examiner has indicated that the rejection should be Barry in view of Huyn.

Claim 49, and its dependent claims (which include Claims 50-51, 53, and 59-61) define a method for creating a database by collecting biological sample and medical data from a least one

donor from at least one collection establishment; deriving proteomic and genomic information from the sample; storing the sample; associating the medical data, proteomic and genomic information with the sample; and performing these steps longitudinally.

As discussed above, Barry teaches a relational database for matching archived medical information to particular diagnosis codes and generating a specific patient report. Huyn teaches a database for storing subject responses to a medical questionnaire.

The combined teachings of Barry and Huyn do not establish a prima facie case of obviousness as the combination does not teach or suggest a number of the recitations of claim 49. MPEP § 2143.

For example, neither reference teaches collecting biological samples or medical data from donors of collection establishments as recited in steps (a) and (b) of Claim 49. Barry collects a single sample from a patient seeking a diagnosis, not from a *donor of a collection establishment*. Similarly, Huyn does not teach collecting biological samples from a donor of a collection establishment but rather is focused on recording answers to medical questions. Likewise, neither reference discloses deriving proteomic and genomic information from a biological sample (step (c)), much less longitudinally (step (f)). Both Huyn and Barry do not teach proteomic or genomic analysis on samples, much less performing this analysis longitudinally. Moreover, neither reference teaches storing biological samples for later recovery (step (d)). Barry teaches using a sample for immediate diagnosis not for storing for later retrieval. Accordingly, the combination of Barry and Huyn fails to teach or suggest a number of the recitations of Claim 49 and, thus, this rejection of Claim 49 and its dependent claims should be withdrawn.

E. Claims 27 and 68

The Examiner has rejected Claims 27 and 68 under 35 U.S.C. §103(a) as being unpatentable over Barry in view of Schappert as applied to Claim 24 and further in view of U.S. Patent No. 5,915,240 to Karpf (Karpf). Claims 27 and 68 depend from Claim 24.

Claims 27 and 68 relate to situations in which the donor is a deferred donor. Applicants acknowledge that the concept of a "deferred donor" was known in the art. As discussed above, Karpf teaches a reference computer system for access to medical information over a computer network. This reference computer system, for example, can be used to look up medical information that must be up-to-date and current such as blood donor deferral criteria. As such, Karpf does not cure the deficiencies of Barry and Schappert discussed above. Karpf does not teach using the reference computer system for collecting and storing biological samples and medical data from donors from collection establishments in order to identify research subjects.

In view of the basic flaws in the Barry and Schappert references, and the fact that Karpf does not provide the missing gaps in these patents, but only provides the term "deferred donor", the Examiner is requested to reconsider and withdraw this rejection.

F. Claims 31-32 and 36-37

The Examiner has rejected claims 31-32 and 36-37 under 35 U.S.C. §103(a) as being unpatentable over Barry in view of Schappert, and further in view of U.S. Patent No. 6,730,477 to Sun (Sun). Claims 31-32 and 36-37 depend from Claim 24.

Claims 31-32 are directed to methods wherein the medical data collected comprises pharmacogenomic or genomic data, or proteomic data respectively. Claims 36-37 are directed to methods wherein the criteria for selecting a research subject include pharmacogenomic or genomic data, or proteomic data respectively. In support of this rejection, the Examiner relies on

Sun (column 6, line 61 to column 7, line 8; column 7, lines 10-23; and column 8, lines 31-49) for the proposition that medical data comprises pharmacogenomic, genomic or proteomic data. Sun is directed to methods for diagnosing, monitoring and staging breast cancer based on analyzing changes in levels of breast specific genes (BSG) in cells. Applicants do not dispute that medical data may include genomic and proteomic data. However, Sun does nothing to overcome the deficiencies of Barry and Schappert since it provides no information on collecting biological samples and medical data from donors from collection establishments and using this information to identify a research subject. Accordingly, Applicants request the Examiner to withdraw this rejection

G. Claims 55-58 and 62-65

The Examiner has rejected claims 55-58 and 62-65 under 35 U.S.C. §103(a) as being unpatentable over Barry et al. in view of Huyn and further in view of Sun. Claims 55-58 and 62-65 depend from Claim 49.

Claims 55 to 58 define the nature of the genomic or proteomic information provided by the method of claim 49. Claims 62 to 65 are directed to methods for identifying a genomic or proteomic characteristic which correlates with a disease by creating a database according to claim 49. Accordingly, all of the rejected claims depend on Claim 49. As discussed above in the Examiner's rejection of Claim 49, neither Barry and Huyn disclose collecting biological samples and medical data from donors from collection establishments. Sun discloses proteomic/genomic monitoring of BSGs. Accordingly, Sun does not cure the deficiencies of the other cited references and therefore cannot be combined with these references to render obvious these claims.

H. Claims 39-42

The Examiner has rejected claims 17-20 and 39-42 under 35 U.S.C. §103(a) as being unpatentable over Barry in view of Schappert, as applied to Claim 24 above.

The Examiner is respectfully directed to the discussion of the rejection of Claim 24 above from which Claims 39-42 depend. Claims 39 to 42 relate to methods which utilize a second database. Given the deficiencies of the Barry and Schappert references, and the requirements of Claims 39-42 which recite the additional requirement of a second database, applicants request this rejection be withdrawn.

Conclusion

The present invention is not taught or suggested by the prior art. Accordingly, applicants request respectfully that the rejection of the claims be withdrawn.

As discussed with the Examiner, the undersigned requests an interview prior to the issuance of another Action.

Respectfully submitted

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